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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,100	01/31/2005	John W. Adams	AREN-027 (027.US2.PCT)	4553

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EXAMINER	
LI, RUIXIANG	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
09/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,100	ADAMS ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *132-139,141 and 143-153* is/are pending in the application.

4a) Of the above claim(s) *148-152* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *132-134, 136-139,141,143-147 and 153* is/are rejected.

7)☒ Claim(s) *135* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/16/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/03/2008 has been entered. Claims 140 and 142 are canceled. Claim 153 is added. Claims 132-139, 141, and 143-153 are pending. Claims 132-139, 141, 143-147, and 153 are currently under consideration. Claims 148-152 are withdrawn from consideration because they are drawn to non-elected invention.

Withdrawn Objections and/or Rejections

The rejection of claims 132-147 under 35 U.S.C. 112, second paragraph is withdrawn in view of amended claims.

The rejection of claims 132-139 and 145-147 under 35 U.S.C. 112, first paragraph for written description and the rejection of claims of 132-134 and 136-147 under 35 U.S.C. 112, first paragraph for written description are with drawn in view of amended claims.

Information Disclosure Statement

The information disclosure statement filed on 09/16/2008 has been considered by the examiner.

Claim Rejections Under 35 U.S.C.§112, 1st Paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 132-134, 136-139, 141, 143-147, and 153 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying an agonist of GPCR of SEQ ID NO: 2 and 3 that has cardioprotective activity, does not reasonably provide enablement for a method of identifying a compound that has cardioprotective activity using a GPCR comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the

claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 132-134, 136-139, 141, 143-147, and 153 are drawn to a method of identifying a compound as having cardioprotective activity, comprising determining whether said compound stimulates a G protein-coupled receptor comprising an amino acid sequence with at least 90% identity to SEQ ID NO: 3. Thus, the claims encompass a method of using a genus of GPCR polypeptides comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 3. Since the claims do not require that GPCR variants or homologues possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature, the claims are broad.

The specification discloses the RUP41 GPCR polypeptides set forth in SEQ ID NO: 2 and 3, and a reduced level of RUP41 transcripts in congestive heart failure (Example 14). The specification also asserts that over-expression of RUP41 promotes survival of neonatal rat ventricular myocytes (NRVMs; Example 16) and rescues NRVMs from hypoxia/reoxygenation (Example 17). However, other than the RUP41 GPCR polypeptides set forth in SEQ ID NO: 2 and 3, the specification fails to disclose any other RUP41 GPCR polypeptides that possess the same physiological role as that of RUP41 GPCR of SEQ ID NO: 3 and can be used in the claimed methods. The specification fails to provide sufficient guidance and/or working examples with respect to

how to make and use the genus of GPCR variants or homologues encompassed in the instant claims.

The specification discloses the amino acid sequence of a first allele of human GPR22, SEQ ID NO: 2, and a second allele of human GPR22, SEQ ID NO: 3. However, there is no description of other mutational sites that exist in nature, and there is no description of how the structure of the polypeptides of SEQ ID NOS: 2 and 3 relates to the structure of different variants. The general knowledge in the art concerning variants does not provide any indication of how the structure of one variant is representative of other unknown variants having concordant or discordant functions. The nature of variants is such that they are variant structures where the structure and function of one does not provide guidance to the structure and function of others.

The prior art (U.S. 6,555,339 B1) teaches a GPR22, which is 99.5% identical to the amino acid sequence of SEQ ID NO: 3, 100% identical to the amino acid sequence of SEQ ID NO: 2 and preparation of a non-endogenous and constitutively activated form of the GPR22 by site-directed mutagenesis (F312K). However, the prior art does not teach the ligand of the GPR22 and the physiological role of the GPR22 and does not provide compensatory structural or correlative teachings to enable one skilled in the art to make the encompassed GPCR variants and homologues that can be used in the instant claimed method.

It is unpredictable whether a GPCR that has 90% sequence identity to SEQ ID NO: 3 shares the same property of RUP41 GPCR of SEQ ID NO: 3 because the instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the recited genus of GPCR variants and homologues. There is no description of the conserved regions that are critical to the structure and function of the genus recited. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. It would take undue experimentation for one skilled in the art to practice the instantly claimed invention.

Accordingly, in view of the various factors, the instant disclosure fails to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

(iii). Response to Applicants' argument

At page7, the 3rd paragraph, Applicants argue that the claims have been amended to recite "(c) identifying a compound as having an activity that stimulates said GPCR". Applicants argue that as such, the amended claims require a functional GPCR having an amino acid sequence having at least 90% identity to SEQ ID NO: 3.

Applicants' argument has been fully considered, but is not deemed to be persuasive because such an amendment does not place a meaningful and specific functional

limitation for the variants and homologues of SEQ ID NO: 3. The mere fact that a GPCR can be stimulated by a compound does not tell the particular function of the GPCR.

At page 7, the 4th paragraph, Applicants request the examiner to reconsider the argument made on page 8-10 of Applicants' prior response where the structure/function relationship of GPCRs was discussed.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the claims do not require that the GPCR variants or homologues possess any particular biological activity nor any particular conserved structure, whereas Applicants' argument on the structure/function relationship of GPCRs in general does not address how to make and use the genus of particular GPCR variants or homologues encompassed in the instant claims.

Claim Objections —Minor Informalities

(i). Claim 135 is objected to because it recites non-elected amino acid sequence of SEQ ID NO: 5 (see office action mailed on 12/21/2006, page 2, the 2nd paragraph). (ii). Claim 144 is objected to because it recites non-elected disease species (other than elected congestive heart failure).

Appropriate correction is required.

Conclusion

No claims are allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
September 21, 2008